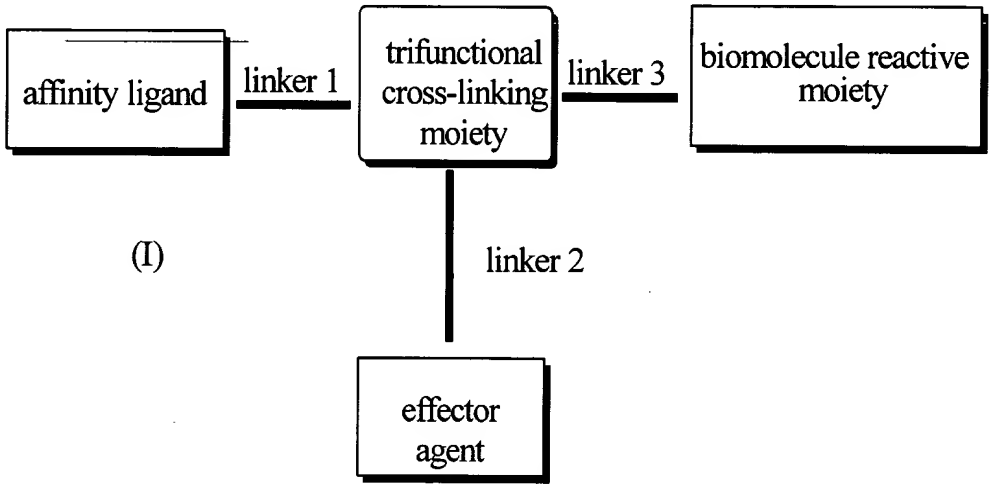
IN THE CLAIMS:

Please amend the claims and add new claim 40 as shown below.

Claim 1 (currently amended): Reagent for conjugation to a biomolecule ~~for diagnosis and treatment of human and animal conditions or diseases~~, wherein the reagent is a single molecule with at least three functional parts and has the following schematic structure (I):



(I)

a) wherein a trifunctional cross-linking moiety is coupled to

b) an affinity ligand via a linker 1, wherein said affinity ligand is biotin, or a biotin derivative having essentially the same binding function to avidin or streptavidin as biotin, said affinity ligand binds with another molecule having affinity for said ligand, and said affinity ligand being connected to said linker 1 via a biotinamide bond which is stabilized towards enzymatic cleavage, to

c) an effector agent, optionally via a linker 2, said effector agent exerting its effect on cells, tissues and/or humorous molecules in vivo or ex vivo, and to

d) a biomolecule reactive moiety, optionally via a linker 3, said moiety forming a covalent bond between the reagent and the biomolecule,

wherein said stability towards enzymatic cleavage of the biotinamide bond has been stabilized by introducing an alpha carboxylate or an N-methyl group in linker 1.

Claim 2 (previously presented): Reagent according to claim 1, wherein the trifunctional cross-linking moiety is selected from the group consisting of triaminobenzene, tricarboxybenzene, dicarboxyaniline and diaminobenzoic acid.

Claim 3 (previously presented): Reagent according to claim 1, wherein the affinity ligand is a moiety that binds with another molecule with an affinity constant of 10^6 M-1 or higher.

Claims 4 and 5 (canceled)

Claim 6 (previously presented): Reagent according to claim 1, wherein the biotin derivative is selected from the group consisting of norbiotin, homobiotin, oxybiotin, iminobiotin, desthiobiotin, diaminobiotin, biotin sulfoxide, and biotin sulfone, or other molecules thereof having essentially the same binding function.

Claim 7 (previously presented): Reagent according to claim 5, wherein the stability towards enzymatic cleavage of the biotinamide bond to release biotin has been improved by using norbiotin or homobiotin.

Claim 8 (previously presented): Reagent according to claim 1, wherein linker 1 serves as an attaching moiety and a spacer between the trifunctional cross-linking moiety and the biotin moiety such that binding with avidin or streptavidin, or a derivative of avidin or

streptavidin having essentially the same binding function to the affinity ligand, is not sterically hindered.

Claim 9 (previously presented): Reagent according to claim 1, wherein linker 1 contains hydrogen bonding atoms, or ionizable groups to aid in water solubilization of the biotin moiety.

Claim 10 (cancelled)

Claim 11 (previously presented): Reagent according to claim 1, wherein the effector agent is selected from the group consisting of synthetic toxins, natural occurring toxins, enzymes that convert a pro-drug to an active drug, immunosuppressive agents, immunostimulating agents, and radionuclide binding/bonding moieties, with or without the radionuclide.

Claim 12 (previously presented): Reagent according to claim 1, wherein the effector agent is a radionuclide binding/bonding moiety to which radionuclides can be bound by chelation or covalent bonding.

Claim 13 (original): Reagent according to claim 7, wherein the effector agent is a radionuclide binding/bonding moiety to which radionuclides can be bound by chelation or covalent bonding.

Claim 14 (currently amended): Reagent according to claim 1, wherein the effector agent comprises aryl halides and vinyl halides for radionuclides of halogens, at least one amino-carboxy compound ~~derivatives~~, and cyclic amines for In, Y, Pb, Bi, Cu, Sm, and Lu radionuclides.

Claim 15 (previously presented): Reagent according to claim 1, wherein the effector agent is provided with positron imaging radionuclides, therapeutic radionuclides, and gamma imaging radionuclides.

Claim 16 (previously presented): Reagent according to claim 1, wherein linker 2 is excluded.

Claim 17 (previously presented): Reagent according to claim 1, wherein linker 2 provides a spacer length of 1-25 atoms or groups of atoms.

Claim 18 (previously presented): Reagent according to claim 1, wherein linker 2 contains hydrogen bonding atoms, or ionizable groups to aid in water solubilization.

Claim 19 (previously presented): Reagent according to claim 1, wherein the biomolecule reactive moiety is selected from the group consisting of active esters, aryl or alkyl imidates, alkyl or aryl isocyanates or isothiocyanates reactive with amino groups on the biomolecule, maleimides or alpha-haloamides reactive with sulfhydryl groups on the biomolecule, aryl and alkylhydrazines or alkyl or aryl hydroxylamines reactive with aldehyde or ketone groups naturally occurring or synthetically produced on the biomolecule.

Claim 20 (previously presented): Reagent according to claim 1, wherein linker 3 is excluded.

Claim 21 (previously presented): Reagent according to claim 1, wherein linker 3 provides a spacer of a length of 1-25 atoms or groups of atoms.

Claim 22 (previously presented): Reagent according to claim 1, wherein linker 3 contains hydrogen bonding atoms, or ionizable groups to aid in water solubilization.

Claim 23 (cancelled)

Claim 24 (original): Reagent according to claim 1, wherein more than one affinity ligand and/or more than one effector agent are bound to a trifunctional or tetrafunctional cross-linking group.

Claim 25 (previously presented): Reagent according to claim 1 for use in targeting of cancer, myocardial infarcts, deep vein thrombosis, stroke loci, pulmonary embolism and atherosclerosis.

Claim 26 (withdrawn): Method for diagnosis or treatment of a mammalian condition or disease, wherein a reagent according to claim 1 is conjugated to a biomolecule, and wherein said conjugated is added to the blood circulation of a mammal and kept therein for a certain of time in order to be concentrated to the target tissue or cells, wherein the biomolecules not being attached to the target tissue are completely or partially removed from the blood circulation by administration of a protein specifically binding to the affinity ligand or by passing the mammalian blood or plasma through an affinity column specifically adsorbing the conjugated biomolecule by specific interaction with the affinity ligand.

Claim 27 (withdrawn): Method for diagnosis or treatment of a mammalian condition or disease, wherein a reagent according to claim 1 provided with a radionuclide is conjugated to a biomolecule, or alternatively, the reagent is conjugated to the biomolecule prior to attachment of the radionuclide, and the said radioactive conjugated biomolecule is added to the blood circulation of a mammal and kept therein for a certain period of time in order to be concentrated to the target tissue or cells, wherein the biomolecules that are not being attached to the target tissue are completely or partially removed from the blood circulation by administration of a protein specifically binding to the affinity ligand or by passing the mammalian blood or plasma through an affinity column specifically adsorbing the conjugated biomolecule by specific interaction with the affinity ligand.

Claim 28 (withdrawn): Kit for extracorporeally eliminating or at least reducing the concentration of a non-tissue-bound therapeutic or diagnostic biomolecule conjugate, which has been introduced to a mammalian host and kept therein for a certain time in order to be concentrated to the specific tissues or cells by being attached thereto, in the plasma or whole blood of the vertebrate host, said kit comprising a therapeutic or diagnostic biomolecule, a reagent for simultaneous conjugation of an affinity ligand and an effector agent to a biomolecule, means for extracoporeal circulation of whole blood or plasma from the vertebrate host, an optional plasma separation device for separation of plasma from blood, an extracoporeal adsorption device, and a means for return of whole blood or plasma without or with the remainder of non-tissue-bound target specific therapeutic or diagnostic agent to the mammalian host, wherein the adsorption device comprises immobilized receptors specific towards an affinity ligand.

Claim 29 (withdrawn): A kit according to claim 28, wherein the effector agent is selected from the group consisting of synthetic toxins, naturally occurring toxins, enzymes, capable

of converting a pro-drug to an active drug, immunosuppressive agents, immunostimulating agents, and radionuclide binding/bonding moieties with or without the radionuclide.

Claim 30 (withdrawn): A kit according to claim 28, wherein the affinity ligand is biotin, or a biotin derivative having essentially the same binding function to avidin or streptavidin as biotin, and the immobilized receptor is avidin or streptavidin, or a derivative of streptavidin having essentially the same binding function to biotin.

Claim 31 (previously presented): Reagent according to claim 9, wherein the hydrogen bonding atoms are ethers or thioethers and the ionizable groups are carboxylates, sulfonates, or ammonium groups.

Claim 32 (currently amended): Reagent according to claim 14, wherein the amino-carboxy ~~derivatives are~~ is EDTA, ~~or~~ DTPA, or a derivative ~~derivatives~~ thereof having substantially the same bonding properties, and the cyclic amines are NOTA, DOTA, or TETA.

Claim 33 (previously presented): Reagent according to claim 32, wherein the DTPA derivatives are Me-DTPA, CITC-DTPA, and cyclohexyl-DTPA.

Claim 34 (previously presented): Reagent according to claims 15, wherein the positron imaging radionuclides are selected from the group consisting of F-18, Br-75, Br-76, and I-124, the therapeutic radionuclides are selected from the group consisting of Y-90, I-131, In-114m, Re-186, Re-188, Cu-67, Sm-157, Lu-177, Bi-212, Bi-213, At-211, and Ra-223, and the gamma imaging radionuclides are selected from the group consisting of Tc-99m, In-111 and I-123.

Claim 35 (previously presented): Reagent according to claim 17, wherein linker 2 provides a spacer length of 16-18 atoms.

Claim 36 (previously presented): Reagent according to claim 18, wherein hydrogen bonding atoms are ethers or thioethers, and the ionizable groups are carboxylates, sulfonates, or ammonium groups.

Claim 37 (previously presented): Reagent according to claim 19, wherein the active esters are selected from the group consisting of N-hydroxy-succinimide esters, sulfo-N-hydroxysuccinimide esters, phenolic esters.

Claim 38 (previously presented): Reagent according to claim 21, wherein linker 3 provides a spacer of a length of 6-18 atoms.

Claim 39 (previously presented): Reagent according to claim 22, wherein the hydrogen bonding atoms are ethers or thioethers and the ionizable groups are carboxylates, sulfonates, or ammonium groups.

Claim 40 (new): Reagent according to claim 1, wherein the reagent comprises:

3-(13'-Thioureabenzyl-CHX-A'')Trioxadiamine-1-(13''-Biotin-N-methyl-Glycyl)trioxadiamine-5-Isothyocyanato-Aminoisophthalate.